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"A Post-Graduate Study."

ALCOHOL
IN ITS
Relationship to Diseases
OF
Bacterial Origin.

AN ADDRESS
BY 1872-
ARTHUR EVANS, M.S., M.D.Lond., F.R.C.S.,
AT THE
42ND ANNUAL BREAKFAST
WITH
THE BRITISH MEDICAL ASSOCIATION,
BIRMINGHAM, 1911.

LONDON:
NATIONAL TEMPERANCE LEAGUE,
Paternoster House, E.C.

1912

THIS BOOKLET

is intended particularly for the perusal of Medical Graduates who have recently entered upon professional work, or are engaged in specialized study at the Hospitals. The address deals with a matter of the utmost importance in relation to D.P.H. work, and indicates the direction of modern research on Alcohol. Delivered under the presidency of Professor Saundby, President, supported by Sir James Barr, President-elect, and Professor Reeve, Toronto, a Past-President, of the B.M.A., the Address made a deep impression on the Medical Men to whom it was delivered at Birmingham.

Sept. 7, 1923 AL.

Alcohol in its Relationship to Diseases of Bacterial Origin.

BY

ARTHUR EVANS, M.S., M.D. (LOND.) F.R.C.S. (ENG.)

THE problem of the entrance of noxious bacteria into the human organism and the defensive mechanism of the organism has been the subject of much recent work, and now possesses an extensive literature; the knowledge we have gained is of far-reaching importance.

During this research work new methods of investigation have been elaborated and new terms coined to explain the phenomena observed and the principles supposed to underlie them. It is necessary we should be conversant with one or two of these before we can appreciate the significance of the alterations in these processes when a disturbing factor, such as alcohol, is introduced.

We have learned that an animal susceptible to a disease can be rendered immune, and also how this can be effected. Thus, if into an animal we inject small and increasing doses of the typhoid bacillus, the animal can be rendered immune to typhoid fever. What has happened?

If some of the blood serum of such an animal be injected with a mixture of typhoid organisms into the peritoneal cavity of a normal guinea pig, and then in half an hour a microscopical examination of the peritoneal exudate be made, it will be found that the microbes are in all stages of dissolution; and to this the name of Bacteriolysis has been given—the serum of the animal has acquired the power of destroying the noxious bacteria; this it has done because there has been developed in it, as a result of the previous inoculations with these same bacteria, something to which the name of immune body, or amboceptor has been given.

The same thing will happen in a test tube if fresh immune serum be added to bacteria; but if the immune serum be kept for some time, or if it be raised to a temperature of 56° C., it loses the power of bacteriolysis. Now, if to this serum which has lost the power of bacteriolysis, some fresh normal serum be added, the power is regained, which shows that in the immune serum there are, at any rate, two factors necessary for this bacteriolytic action, one the immunising body or amboceptor, stable, specific, found only, or in greater quantity, after the treatment of an animal with the particular microbe, and another which is also contained in normal serum and exudates, unstable, destroyed by a temperature of 56% C., and to this the name of complement is given.

Now if the question be asked; Will an animal recover if infected with a particular microbe? the answer must depend upon whether it can develop the specific immune body—its bacteriolytic amboceptor—and whether there be sufficient complement present.

In investigating the formation of immune bodies, and the presence of complement, a process analagous to bacteriolysis is commonly used by investigators—namely, that of hæmolysis.

We know that the blood serum of some animals can hæmolyse (can destroy) the red corpuscles of other species of animals; but this is not universally so; thus, the serum of a guinea pig has no action on the red corpuscles of the rabbit, but after a few injections of rabbit's red corpuscles into a guinea pig, it is found

that the guinea pig's serum has acquired the power of hæmolysing the rabbit's red corpuscles, just as an animal formerly destitute of the power becomes able to dissolve the cholera vibrio, or typhoid bacillus, after a few injections of these organisms; and whereas in this latter case we have found the power to reside in the bacteriolytic amboceptor and the complement, so in the former we find that the power of hæmolysis is dependent on the formation of a hæmolytic amboceptor, plus the complement already existing in the serum.

Here, then, in the hæmolysis of red corpuscles on the one hand, and in bacteriolysis on the other, we have an accurate method of estimating the potency of the amboceptor and complement present in a given serum, and, too, an accurate method of estimating the effect produced on the potency of these bodies by the administration of a given agent; for the measure of hæmolysis or bacteriolysis of a given blood serum, before and after the administration of a given agent, is the measure of this agent's effect on the formation of the amboceptor and complement. What do we learn when these tests are applied to alcohol?

Let us now look at the results of a large series of experiments most carefully performed by Professor Laitinen, of Helsingfors, and contained in his lecture on the Influence of Alcohol on Immunity, which although delivered at the International Congress on Alcoholism in London in 1909, I believe is unknown not only to the average medical man, but even to those in the profession who devote a large part of their time to the study of the blood serum, and serum and vaccine therapy; and believing this, and recognising the importance of the results obtained, I am glad of this opportunity afforded me by the National Temperance League of speaking here this morning, and I believe I am using it to its fullest advantage by bringing before your attention Laitinen's work.

First, we know that human blood serum can hæmolyse the red blood corpuscles of a rabbit ; it therefore contains the necessary hæmolytic amboceptor and complement. Does the taking of alcohol affect this hæmolytic power?

He experimented with the blood serum from 31 drinkers and from 35 abstainers.

By drinker he means "a person who takes alcohol in any quantity whatever" ; many of these "drinkers" were in fact "most moderate consumers of alcohol."

Influence of Alcohol on the Hæmolytic Power of the Human Blood Serum.

A five per cent. suspension of rabbit's blood corpuscles was taken, and to this was added human blood serum in various dilutions; the following table shows the percentage of hæmolysis of the rabbit's corpuscles.

Dilutions of Blood Serum		.4	.1	.04	.01	.004
Average percentage of Hæmolysis	Drinkers ...	80·32	35.42	5.87	1.29	.09
	Abstainers	82.29	45.79	5.33	1.19	.63

Here the average percentages of results on both sides clearly tend to prove that the hæmolytic power of sera from drinkers was weaker than that from abstainers; in other words the alcohol has lessened the amboceptor and complement content of the serum.

Laitinen next examined the hæmolytic power of the blood serum in six women who were abstainers, and later examined the same individuals when for 63 days they had taken from 8 to 10 c.cm, of a 10 per cent. wine daily (equivalent to 2⅘-3½ ounces of Claret or Burgundy).

A ten per cent. suspension of the rabbit's corpuscles was used, and to this was added human blood serum in various dilutions.

Dilutions of Blood Serum		.4	.1	.04	.01
Average percentage of Hæmolysis	Whilst Abstainers	89.17	61.67	7.58	2.25
	After use of Alcohol	79.17	35.0	7.08	1.33

This table shows clearly the marked diminution in the hæmolytic power of the blood serum produced by the ingestion of small quantities of alcohol.

Now, taking three persons, each over fifty years of age and all well known to the investigator, and using a five per cent. suspension of rabbit's corpuscles and various dilutions of the human serum, the following results were obtained ;

Dilutions of Blood Serum		·4	·2	·1	·06	·02
Percentage of Hæmolysis	Drinker	80	70	30	8	1
	Moderate ...	90	50	30	20	1
	Abstainer ...	85	75	70	40	2

Another series of experiments on the resistive power of human red corpuscles in the presence of a heterogeneous serum also showed very clearly the profound effect produced on the blood by the consumption of alcohol.

The Action of Alcohol on the Resistive Power of Human Red Blood Corpuscles.

Red blood corpuscles were obtained from 27 drinkers and 27 abstainers, and a ten per cent. suspension of each person's corpuscles was made ; to this was added various dilutions of normal rabbit serum, and the amount of hæmolysis was estimated; the following table clearly shows the diminished resistivity of the red corpuscles of a drinker when compared with those of an abstainer :

Dilution of Normal Rabbit Serum		.4	.3	.1	.01
Average Percentage of Hæmolysis	Drinkers ...	44.00	33.06	12.35	0.24
	Abstainers ...	42.46	31.85	11.37	0.04

The same experiment was made with the red blood corpuscles of six women who were total abstainers, and repeated at a later date when for 63 days they had taken 8-10 c.cm. of alcohol daily (equivalent to 2⅘-3½ ounces of Claret or Burgundy); the diminution in resistivity of red blood corpuscles occasioned by the drinking of this "moderate" amount of alcohol is very striking :

Dilution of Rabbit Serum		.4	.3	.1
Average Percentage of Hæmolysis	Whilst Abstainers ...	48.33	42.00	13.25
	After using Alcohol	67.50	48.33	20.08

The experiment was then varied by using immune serum from rabbits, which serum had been incubated at 56°C. to remove the complement; to this, in order to supply the necessary complement, fresh guinea-pig serum was added; using ten per cent. suspensions of human red corpuscles obtained from 16 drinkers and 16 abstainers, and various dilutions of immune serum, the following results were obtained.

Dilutions of Immune Rabbit Serum		.06	.04	.01	.001	.0004
Average Percentage of Hæmolysis	Drinkers ...	67.81	48.94	17.31	3.47	2.77
	Abstainers ...	60.19	48.25	16.75	3.06	2.38

The same experiment as above, using the red blood corpuscles of three persons well known to the investigator gave the following results:

Dilution of Immune Sheep Serum		.06	.04	.01	.001	.0004
Percentage of Hæmolysis	Drinkers ...	55	35	20	7	7
	Moderate ...	45	25	10	5	5
	Abstainers ...	25	13	8	3	3

In all these cases—94 individuals—carefully examined in four different series of tests, the results agree that: the resistive power of human red corpuscles against a heterogeneous normal serum, or against an immune serum, is somewhat lessened by the consumption of alochol.

Laitinen also performed a large number of experiments to estimate the amount of complement present in the blood serum of those who took alcohol and of those who did not.

He took 1 c.cm of five per cent. suspension of human red corpuscles and to this added .1 c.cm of amboceptor serum (made by immunising sheep with human red corpuscles—then raising to 56°C. to remove the complement). This was now fixed by keeping at 37°C. for half an hour, and then washed in isotonic salt solution to remove any amboceptor not fixed by the red corpuscles.

To furnish the complement necessary for hæmolysis he added human blood serum from various individuals the measure of whose complement-content was to be determined. The relative amounts of hæmolysis was the measure of the complement-content—and Laitinen sums up the results by saying "that the average complement-content of blood serum from the remarkable number of persons used in my experiments was greater in the majority of the different dilutions in the case of abstainers than in that of drinkers." [The total number of different persons experimented upon by Laitinen was 223; from 9 to 16 separate tests being taken in the case of each person.]

THE BACTERICIDAL POWER OF BLOOD SERUM FROM ALCOHOL-DRINKERS AND ABSTAINERS.

To determine the bactericidal power of blood serum 1 c.cm of fresh blood serum was taken, and into this was mixed a platinum loop dipped in a 24-hour-old suspension of bacillus typhosus in bouillon. The various blood sera treated similarly were placed in an incubator at 37°C. After 1, 2, 6 and 24 hours respectively, by means of a normal platinum needle loop (.002 milligram) gelatine cultures were laid in Petri's dishes and the bacteria colonies which grew during the five following days were counted:

Number of hours bacteria in contact with blood serum		1 hour	2 hours	6 hours	24 hours.
Average number of bacteria colonies in	19 Drinkers	19996.84	337.18	77.37	2.67
	11 Abstainers	1858.7	208.4	15,37	1,45

That is: The blood serum from abstainers was more bactericidal than that from drinkers.

I shall not speak of phagocytosis, as the part the phagocytes play in the destruction of pathogenic organisms and in the cure of infectious diseases has been well known for many years. So, too, is it well known, as the result of numerous experiments by various workers, and as clinical experience fully confirms, that alcohol diminishes the number of leucocytes and their power of leucocytosis.

I dare not, however, omit reference to another important factor in the interaction between the body cells and bacteria. I allude to our new friends—Sir Almroth Wright's opsonins.

Through him and his fellow workers we have learned that the polymorphonuclear leucocytes do not freely take up and digest bacteria unless certain substances are present in the serum—the opsonins—and, regarding phagocytosis as the main process by which bacteria are destroyed within the organism, and the opsonins as the means whereby the bacteria are prepared for ingestion, Wright has concluded that the relative amount of opsonins in a given serum gives an indication of the defensive powers of the individual ; for the purpose he has established an "opsonic index"—made by dividing the number of bacteria found in a certain number of leucocytes in an emulsion made with the patient's blood, by the number of bacteria in the same number of leucocytes in an emulsion made with normal serum. The principle of vaccine therapy is to increase the opsonic power of the blood serum, and so increase its fighting capacity, that is, its power of defeating bacterial invasion.

Do we know anything respecting the effect produced on the opsonic index by the ingestion of alcohol ? Not so much as we ought to know, but what we do know is instructive.

Experiments by Prof. Charles Stewart, of the American Medical Missionary College, on the influence of alcohol internally on the opsonic power of the blood, showed, in the four individuals experimented on, that, after taking two ounces of port wine, there was an average fall in the opsonic index for tubercle bacillus of 37 per cent., and for streptococcus an average fall of 42 per cent.

I would like to quote from Emery's "Immunity and Specific Therapy." "The liability of alcoholic subjects to pneumonia, and some other infective diseases is well known, and in them the prognosis is more than usually unfavourable. It is known to destroy certain delicate substances (complements and opsonins) which play some part in the defence of the body against microbic invasion but it is not known whether these effects are actually manifested in the circulating blood." Thanks to Laitinen we now know that the last sentence must read, "and it *is* known that these effects are actually manifested in the circulating blood."

If amboceptors, complements, and opsonins are so vitally important in the struggle against disease as the experts tell us—and who are we to dare dispute ? mere physicians and surgeons and pathologists !—and if the destruction of bacteria be only possible in the presence of immune body and opsonins and complement, and if, as has been proved, the taking of alcohol, even in comparatively small quantities, hinders the formation of these defensive agents (and, remember, some of Laitinen's work was done on people who took what practically amounts to 2⅘-3½ ounces of claret or burgundy a day, and that I am given to understand, is "strictly moderate"),—I think I am logically stating the case when I say that the taking of alcohol, even in so-called "moderation," is an invitation to bacterial invasion,

Did the conclusions arrived at as a result of these experiments run counter to the accumulated experience of the past, we might be sceptical, but what the hæmatologists have taught us is strictly in keeping with clinical experience—take only two infective organisms, tubercle bacillus and pneumococcus.

Every modern teacher recognises the close inter-relation between alcohol consumption and tuberculosis. Bauderon has pointed out that in those districts in France where the consumption of alcohol works out at 12·15 litres per person per annum, the death-rate from tuberculosis is 3·3 per 1,000 inhabitants, but where the amount drunk is 35.4 litres per person per annum, the death-rate is 10·8 per 1,000 ; and so forcibly did this inter-relation appeal to the International Congress on Tuberculosis in 1905, that this resolution was passed: "That in view of the close connection between alcoholism and tuberculosis this Congress strongly emphasises the importance of combining the fight against tubercle with the struggle against alcoholism." And now that we, as a nation, are girding ourselves for battle against this white man's plague, let us see to it that we do not forget the dual enemy.

I know it can be said, with all truth, that other factors play a part: poverty, neglect, insanitary surroundings and over-crowding; but surely this does not minimise the part played by alcohol with regard to tubercle, it rather emphasises it, for poverty and overcrowding follow in the train of alcohol.

With regard to the pneumococcus, let us quote from Osler and McCrae, 1910, and combine the mortality tables for pneumonia. "It has long been known that habitual drunkards have a very slim chance of recovery when attacked by pneumonia, and it is noted that the mortality among moderate drinkers is higher than among total abstainers.

Mortality rate in pneumonia: Total abstainers, 18·5 per cent.; moderate drinkers, 25·4 per cent.; intemperate, 52·8 per cent. "This fact," says Osler, "has long been known to life insurance companies as holding good for many diseases other than pneumonia."

How do insurance companies know? I have just received a report from a Life Insurance Office whose boast is that the death rate in the General Section is very low, "consequent upon the careful class of lives cultivated," and I see that the actual deaths as compared with the expected deaths were in the General Section 81·627, and in the Temperance Section, 45·86 per cent.

Before I conclude I desire to call attention to the part which alcohol plays in regard to a special group of

bacterial infections, viz., venereal diseases. The importance of this subject can not be better emphasised than by quoting from Sir James Barr's address in medicine at the annual meeting of the Canadian Medical Institution: "During the last 40 years, in England and Wales, the number of deaths due to venereal diseases has fallen from 92·6 to 48 in the 1,000,000 population. So far as these statistics are reliable, they seem to me to point to a great improvement in the treatment, as there is no reason to believe that there has been any diminution in the incidence. These diseases from their deteriorating effects on the race, merit the attention of a statesman. A determined attempt should be made to stamp them out. The suffering caused to innocent wives and children by those diseases call aloud for their elimination. With a combined international effort they might be stamped out." Then, if they might, they ought to be stamped out!

But till the international stamping-out effort has been put in action, is there anything to be done? Yes. Listen to what that great English pathologist. Professor Mott, says: "Drink is not only the cause of a great number of crimes, but of great misery and human suffering; it causes disease, and accelerates and aggravates diseases caused by pathogenic organisms, *i.e.*, tuberculosis and syphilis; moreover, *it is the indirect cause of venereal infection in a large proportion of the cases*." Here, then, we can help to eliminate, by recognising how fresh infections take place and by acting accordingly.

There is no doubt that even a little alcohol stimulates the animal passions; there is no doubt that even a little alcohol dulls the highest mental capacities of judgment, of cold, calm, deliberate purpose; it dulls the sense of what is right and wrong—in a word the highest and the best in our cerebration is off the throne, the lower and the worse rules for the time. To quote Sir T. S. Clouston

"As a physiological fact all these toxins (alcohol, opium, cocaine, &c.) act first on the power of control and the moral sense, which are the highest and latest evolved qualities in man."

There is no need that I should say more than give you these quotations, but I emphasise this: these first effects of alcohol on the brain occasion a situation of such grave peril that everyone ought to know of it. Time does not permit me to elaborate this subject so I crowd my meaning into a sentence: when a young life starts out from the shelter of home to fight the battles that must be fought and brave the dangers that must be faced, one of the most priceless possessions, one of the greatest safeguards he, or she can have, is that of total abstinence from all alcoholic liquor.

This, I think, is one of the saddest things that can be said about alcohol: that many a life that otherwise had kept its purity, but now inhabits the underworld of our social system, entered the pathway that leads to the gutter whilst under the influence of alcohol; and there, sooner or later infected, becomes a source of infection to other lives trooping that way, led on by the king of the carnival —alcohol.

We do not stake our all on opsonins—the opsonins of to-day may be the obsoletes of to-morrow, but if we examine the opsonic index, or the blood serum with regard to its amboceptor and its complement content, or the collected statistics of clinical investigation, or the report of a Life Insurance Office, or even if we walk the streets with eyes not absolutely blind, we find the same fact outstanding; and, if the whole truth on this subject can be expressed in a sentence, here is the sentence—

ALCOHOL IS THE ALLY OF DISEASE AND DEATH.

THE NATIONAL TEMPERANCE LEAGUE.

INSTITUTED 1856.

THE NATIONAL TEMPERANCE LEAGUE is the pioneer of scientific investigations into the nature and effects of alcohol, having convened the first gathering of medical men for the purpose fifty years ago, when there was inaugurated that great movement of progressive research which has changed the attitude of the whole profession towards the use of this toxic agent.

THE LEAGUE has encouraged such inquiry by influencing scientific opinion at the Annual Meetings of the British and British Medical Associations, and the Royal Sanitary Institute, as well as by the publication of *The Medical Temperance Journal*, in which a most valuable discussion of the subject was carried on for twenty years.

A DECLARATION signed by the Presidents of the Royal Colleges of Physicians and Surgeons, and by 267 leading members of the profession, made in 1871, and the Cantor Lectures on "Alcohol," at the Royal Society of Arts, by Sir B. W. Richardson, M.D., F.R.S., in 1874-5, for both of which the League was responsible, made a great impression and carried forward the work of research in the Medical Schools.

THE SCIENCE AND EDUCATION COMMITTEE

of the League has recently published a Report upon its Research work carried on under the supervision of Dr. W. H. R. Rivers, F.R.S., upon "The Action of Alcohol on Muscular and Mental Efficiency," a copy of which will be sent upon application as under. It indicates clearly the desire of the League to pursue research upon unbiassed lines, and as true "seekers after truth."

Recognising that no measure to obtain the most recent and accurate evidence should be neglected, the Committee hope, as funds permit, to encourage further research by offering grants in aid to graduates or post-graduates in the Medical Schools, who will undertake specialised investigations as to the effects of Alcohol on the Human Organism.

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